PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
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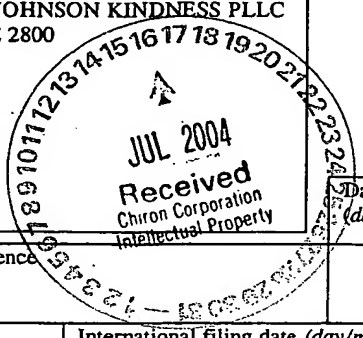

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Applicant's or agent's file reference CHIR-1-20669	Date of Mailing (*day/month/year*) 06 JUL 2004
	IMPORTANT NOTIFICATION

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US03/06742	03 March 2003 (03.03.2003)	01 March 2002 (01.03.2002)

Applicant

CHIRON CORPORATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450	Donna Jagoe
Facsimile No. (703) 305-3230	Telephone No. (571) 272-0600

Form PCT/IPEA/416 (July 1992)

PROCESSED DOCKETING
MAS JUL 08 2004 MD
CHRISTENSEN, O'CONNOR JOHNSON & KINDNESS

DOCKETED on/by 7/16/04 ou
Atty. GS PA
File # PP19016.002
Due Date _____ Ext _____
Final Date _____

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CHIR-1-20669	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/06742	International filing date *(day/month/year)* 03 March 2003 (03.03.2003)	Priority date *(day/month/year)* 01 March 2002 (01.03.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 38/16 and US Cl.: 514/12		
Applicant CHIRON CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 20 August 2003 (20.08.2003)	Date of completion of this report 10 June 2004 (10.06.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Donna Jagoe Telephone No. (571) 272-0600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/06742

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-49 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the claims:
pages 50-56 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the drawings:
pages 1-2 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/06742

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-56	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-56	NO
Industrial Applicability (IA)	Claims 1-56	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-4, 11, 17, 36, 48-50 and 54 lack an inventive step under PCT article 33(3) as being obvious over Sanofi-Synthelabo. Sanofi-Synthelabo teaches administration of GSK3 inhibitors to treat cerebrovascular accidents(see abstract). It further teaches that the GSK3 inhibitors may be supplemented with an active ingredient of another medicament for the treatment of the above mentioned diseases (cerebrovascular accident). Adminstration of the GSK3 inhibitors is *inter alia* intracerebrally and orally(page 6, line 58 to page 7, line 31). The timing of the agent to be administered would have been obvious as it is usual to adminster therapeutic agents as soon as possible in the event of a cerebrovascular accident.

Claims 1, 17, 36, 48-50 and 54 lack an inventive step under PCT article 33(3) as being obvious over Eldar-Finkelman. The prior art teaches GSK-3 inhibitors to be useful of treatment of biological conditions mediated by GSK-3 activity such as treatment of conditions of ischemic insult such as cerebral stroke to prevent, halt or reduce neuronal cell death (page 4, paragraph 0042). Formulations are administered parenterally as well as enterally (page 8, paragraph 0081). Co-administraton of another agent known to treat the biological condition is disclosed on page 7, paragraph 0069. The timing of the agent to be administered would have been obvious as it is usual to adminster therapeutic agents as soon as possible in the event of a cerebrovascular accident.

Claims 1, 17, 36, 48-50 and 54 lack an inventive step under PCT article 33(3) as being obvious over Sanofi-Synthelabo. Sanofi_Synthelabo teaches administration of GSK3 inhibitors to treat cerebrovascular accidents(page 2, lines 10-19). It further teaches that the GSK3 inhibitors may be supplemented with an active ingredient of another medicament for the treatment of the above mentioned diseases (cerebrovascular accident). Adminstration of the GSK3 inhibitors is *inter alia* intracerebrally and orally(page 20, line 33 to page 21, line 33). The timing of the agent to be administered would have been obvious as it is usual to adminster therapeutic agents as soon as possible in the event of a cerebrovascular accident.

Claims 1-56 lack an inventive step under PCT article 33(3) as being obvious over Nuss et al. Nuss et al. teach GSK 3 inhibitors to treat *inter alia* brain injury (see abstract) such as cerebral ischemia (page 1, paragraph 0001). The GSK3 inhibitors can be administered with other therapeutically active agents known to treat cerebral ischemia. The compounds can be administered enterally and parenterally (page 12, paragraph 0102). The timing of the agent to be administered would have been obvious as it is usual to adminster therapeutic agents as soon as possible in the event of a cerebrovascular accident.